What is claimed is:

1. A sensor composition comprising at least one small molecule metabolic reporter (SMMR), wherein the composition is applied to at least one surface of living tissue, organs, interstitial fluid, and whole organisms and transported into the tissue at an effective concentration, wherein when the at least one small molecule metabolic reporter is brought in contact with one or more specific metabolites, a change in fluorescence or absorption of the at least one small molecule metabolic reporter occurs, thereby allowing quantification of the change in fluorescence or absorption, thereby providing detailed *in vivo* information regarding picomolar through millimolar levels of cellular metabolites and metabolic precursors in the living tissue, organs, interstitial fluid, and whole organisms.

2. The sensor composition of claim 1, wherein the at least one small molecule metabolic reporter is selected from the group consisting of a fluorophore, a protein labeled fluorophore, a protein comprising a photooxidizable cofactor, a protein comprising another intercalated fluorophore, a mitochondrial vital stain or dye, and a dye exhibiting at least one of a redox potential, a membrane localizing dye, a dye with energy transfer properties, a pH indicating dye, a coumarin dye, a derivative of a coumarin dye, an anthraquinone dye; a cyanine dye, an azo dye; a xanthene dye; an arylmethine dye; a pyrene derivative dye and a ruthenium bipyridyl complex dye.

3. The sensor composition of claim 1, wherein the one or more specific metabolites are selected from the group consisting of glucose, lactate, H^+, Ca^{2+}, Mg^{2+}, Na^+, K^+, ATP, ADP, P_i, glycogen, pyruvate, NAD(P)+, NAD(P)H, FAD, $FADH_2$, and O_2.

4. The sensor composition of claim 1, wherein the information obtained is selected from the group consisting of assessment of metabolic function; diagnosis of metabolic disease state; monitoring and control of disease state; stress status of cells, tissues and organs; determination of vitality and viability of cells based on metabolic function; critical care monitoring; determination of metabolic concentration; cancer diagnosis; cancer detection; cancer staging; and cancer prognosis.

5. The sensor composition of claim 4, wherein the assessment of metabolic function provides detailed information about glucose metabolism, fructose metabolism or galactose metabolism.

6. The sensor composition of claim 4, wherein the diagnosis of metabolic disease state provides detailed information on advanced-glycosolated end products.

7. The sensor composition of claim 4, wherein the monitoring and control of diseases is related to diabetes, cancer, stress or organ transplantation.

8. The sensor composition of claim 2, wherein the mitochondrial vital stain or dye is a polycyclic aromatic hydrocarbon dye selected from the group consisting of: rhodamine 123; di-4-ANEPPS; di-8-ANEPPS; $DiBAC_4(3)$; RH421; tetramethylrhodamine ethyl ester, perchlorate; tetramethylrhodamine methyl ester, perchlorate; 2-(4-(dimethylamino)styryl)-*N*-ethylpyridinium iodide; 3,3'-dihexyloxacarbocyanine, 5,5',6,6'-tetrachloro-1,1',3,3' -tetraethyl-benzimidazolylcarbocyanine chloride; 5,5',6,6'-tetrachloro-1,1',3,3' -tetraethyl-benzimidazolylcarbocyanine iodide; nonylacridine orange; dihydrorhodamine 123 dihydrorhodamine 123, dihydrochloride salt; xanthene; 2',7'-bis-(2-carboxyethyl)-5-(and-6)-carboxyfluorescein; benzenedicarboxylic acid; 2(or 4)-[10-(dimethylamino)-3-oxo-3-H-benzo[c]xanthene-7-yl]; and iodine dissolved in potassium iodide.

9. The sensor composition of claim 2, wherein the protein labeled fluorophore is at least one of Glucose Oxidase-Labeled Fluorophore (GO-LF) and Glucose Oxidase-Intercalated Fluorophore (GO-IF).

10. The sensor composition of claim 2, wherein the protein comprising a photooxidizable cofactor is Glucose Oxidase (GOx) with a flavin adenine dinucleotide (FAD) in the triplet state ($GOx\text{-}^3FAD^*$).

11. The sensor composition of claim 1, wherein the sensor composition is formulated as a cream, emulsion, ointment, oil, disposable gel film patch, reservoir device or paint.

12. The sensor composition of claim 1, wherein the sensor composition is transported within the skin using at least one technique selected from the group consisting of: electroporation, solvent transport, tattooing, injecting, and passive transport.

13. The sensor composition of claim 1, wherein the quantification of the change in fluorescence or absorption is monitored using fluorescence or absorption spectroscopy.

14. The sensor composition of claim 1, wherein the effective concentration is selected from the group consisting of at least between 0.01 to 500 μg/ml, between 0.1 to 500 μg/ml, between 1.0 to 150 μg/ml, between 1 to 100 μg/ml, and between 10 to 100 μg/ml.

15. The sensor composition of claim 1, wherein a specific application comprises a 5 μL volume of a 400 μM SMMR solution, or a 10 μL volume at 200 μM concentration.

16. The sensor composition of claim 1, wherein the one or more metabolites directly report on and relate to *in vivo* blood glucose levels.

17. The sensor composition of claim 1, wherein the at least one small molecule metabolic reporter is chosen based on one or more properties selected from the group consisting of molecular size, charge, structure, pKa, solubility, polarity, and solvent system used to transport the one or more small molecule metabolic reporters to living tissue.

18. A method for identifying a small molecule metabolic reporter (SMMR) suitable for use in a sensor composition, the method comprising:

delineating the one or more metabolites required to characterize a selected metabolic pathway in a living system;

determining a basic mechanism of action for the SMMR;

selecting one or more wavelength choices for excitation and emission of the SMMR for analysis of absorption and fluorescence measurements;

selecting a molecular structure to meet quantum efficiency and yield requirements;

selecting location, diffusion rate, and duration or lifetime of the SMMR within a tissue or organ layers;

selecting toxicity requirements and limitations; and

optionally relating measured real-time metabolic conditions to disease state for diagnostics or patient care,

thereby identifying a small molecule metabolic reporter for use in a sensor composition.

19. An *in vivo* method for determining the metabolic health and well-being in living organisms, the method comprising:

applying at least one small molecule metabolic reporter (SMMR) to a surface of an organ for a predetermined period of time;

causing penetration of the SMMR to a depth of about 10 μm to about 300 μm;

monitoring a change in the fluorescence or absorption based upon peripheral or epithelial tissue metabolite levels; and

correlating the metabolite levels within peripheral or epithelial tissue with cellular metabolite levels,

thereby determining the metabolic health and well-being in living organisms.

20. An *in vivo* method for monitoring and controlling disease states that affect metabolic processes in living organisms, the method comprising:

applying at least one small molecule metabolic reporter (SMMR) to at least one surface of a living tissue, organs, and/or whole organisms for a predetermined period of time;

causing penetration of the SMMR to a depth of about 10 μm to about 300 μm;

monitoring a change in the fluorescence or absorption based upon peripheral or epithelial tissue metabolite levels; and

correlating the metabolite levels within peripheral or epithelial tissue with cellular metabolite levels,

thereby monitoring and controlling disease states that affect metabolic processes in living organisms.

21. The method of claim 20, wherein the disease states are selected from the group consisting of diabetes, diabetes progression, aging, critical care states, organ transplantation, tissue and cell viability and vitality, cancer diagnosis, cancer detection, cancer staging and cancer prognosis.

22. An *in vivo* method for monitoring the concentration of one or more metabolites or analytes, the method comprising:

applying at least one small molecule metabolic reporter (SMMR) to at least one surface of a living tissue, organs, and/or whole organisms for a predetermined period of time;

causing penetration of the SMMR to a depth of about 10 μm, wherein said depth corresponds with the bottom of the dead stratum corneum layer, to about 175 μm, wherein said depth corresponds with the top of the dermal layer, into the epidermis; and

monitoring a change in the concentration of the one or more metabolites or analytes in a metabolic pathway by detecting changes in the at least one SMMR at one or more time points using an optical reader.

23. The method of claim 22, wherein the SMMR comprises a mitochondrial stain sensitive to membrane potential or chemical gradient.

24. The method of claim 23, wherein the mitochondrial stain is a polycyclic aromatic hydrocarbon dye selected from the group consisting of: rhodamine 123; di-4-ANEPPS; di-8-ANEPPS; $DiBAC_4(3)$; RH421; tetramethylrhodamine ethyl ester, perchlorate; tetramethylrhodamine methyl ester, perchlorate; 2-(4-(dimethylamino)styryl)-N-ethylpyridinium iodide; 3,3'-dihexyloxacarbocyanine, 5,5',6,6'-tetrachloro-1,1',3,3' -tetraethyl-benzimidazolylcarbocyanine chloride; 5,5',6,6'-tetrachloro-1,1',3,3' -tetraethyl-benzimidazolylcarbocyanine iodide; nonylacridine orange; dihydrorhodamine 123 dihydrorhodamine 123, dihydrochloride salt; xanthene; 2',7'-bis-(2-carboxyethyl)-5-(and-6)-

carboxyfluorescein; benzenedicarboxylic acid; 2(or 4)-[10-(dimethylamino)-3-oxo-3-H-benzo[c]xanthene-7-yl]; and iodine dissolved in potassium iodide.

25. The method of claim 22, wherein the at least one SMMR comprises a dye or stain that transfers energy from a molecule generated as a result of the oxidative metabolic pathway and that has a stoichiometric or highly correlated relationship with glucose concentration.

26. The method of claim 22, wherein the at least one SMMR comprises a dye selected from the group consisting of: coumarin; derivatives of coumarin; anthraquinones; cyanine dyes; azo dyes; xanthene dyes; arylmethine dyes; pyrene derivatives; and ruthenium bipyridyl complexes.

27. The method of claim 22, wherein the at least one SMMR comprises a protein labeled fluorophore.

28. The method of claim 27, wherein the protein labeled fluorophore is at least one of Glucose Oxidase-Labeled Fluorophore (GO-LF) and Glucose Oxidase-Intercalated Fluorophore (GO-IF).

29. The method of claim 22, wherein the at least one SMMR comprises a protein comprising a photooxidizable cofactor.

30. The method of claim 29, wherein the protein comprising a photooxidizable cofactor is Glucose Oxidase (GOx) with a flavin adenine dinucleotide (FAD) in the triplet state (GOx-^{3}FAD*).

31. The method of claim 22, wherein the one or more metabolites or analytes is selected from the group consisting of: glucose; lactate; hydrogen ion (H^+); calcium ion (Ca^{2+}) pumping rate; magnesium ion (Mg^{2+}) pumping rate; sodium ion (Na^+) pumping rate; potassium ion (K^+) pumping rate; adenosine triphosphate (ATP); adenosine diphosphate

(ADP); the ratio of ATP to ADP; inorganic phosphate (P_i); glycogen; pyruvate; nicotinamide adenine dinucleotide phosphate, oxidized form (NAD(P)+); nicotinamide adenine dinucleotide phosphate, reduced form (NAD(P)H); flavin adenine dinucleotide, oxidized form (FAD); and flavin adenine dinucleotide, reduced form ($FADH_2$); and oxygen (O_2) utilization.

32. The method of claim 22, where monitoring the change in metabolite or analyte concentration comprises detecting at least one wavelength above 350 nm.

33. The method of claim 22, wherein the SMMR is formulated as a cream, emulsion, ointment, oil, disposable gel film patch, reservoir device or paint.

34. The method of claim 22, wherein the SMMR penetrates within the skin using at least one technique selected from the group consisting of: electroporation, solvent transport, tattooing, injecting, and passive transport.

35. The method of claim 22, wherein the quantification of the change in fluorescence or absorption is monitored using fluorescence or absorption spectroscopy.

36. An *in vivo* method for measuring metabolite levels, said method comprising monitoring in a population of cells one or more relevant metabolites, parameters or analytes in at least one metabolic pathway, wherein the monitoring comprises measuring the fluorescence spectrum emitted by at least one small molecule metabolic reporter (SMMR), wherein at least one fluorescence spectrum emitted by the SMMR is stoichiometrically related to the metabolite, parameter or analyte concentration in the population of cells, whereby analyzing the relatedness provides the *in vivo* metabolite level.

37. The method of claim 36, wherein the population of cells has a predominantly glycolytic metabolism or can be induced to have a glycolytic metabolism.

38. The method of claim 37, wherein the population of cells is located in the epidermis, wherein the epidermis comprises a dynamic, metabolically homogeneous, and homeostatic population of cells.

39. The method of claim 37, wherein the population of cells having a glycolytic metabolism comprise live keratinocytes.

40. The method of claim 39, wherein the live keratinocytes are present in the epidermal layer of skin.

41. The method of claim 40, wherein the live keratinocytes are present at a depth from the surface of the skin from about 10 μm, wherein said depth corresponds with the bottom of the dead stratum corneum layer, to about 175 μm, wherein said depth corresponds with the top of the dermal layer.

42. The method of claim 36, wherein the metabolic pathway is monitored within the population of cells via measurement of one or more specific metabolite or analyte of the glycolytic pathway that has a stoichiometric or highly correlated relationship with glucose concentration.

43. The method of claim 42, wherein the one or more relevant metabolites or analytes are selected from the group consisting of: glucose; lactate; hydrogen ion (H^+); calcium ion (Ca^{2+}) pumping rate; magnesium ion (Mg^{2+}) pumping rate; sodium ion (Na^+) pumping rate; potassium ion (K^+) pumping rate; adenosine triphosphate (ATP); adenosine diphosphate (ADP); the ratio of ATP to ADP; inorganic phosphate (P_i); glycogen; pyruvate; nicotinamide adenine dinucleotide phosphate, oxidized form (NAD(P)+); nicotinamide adenine dinucleotide (phosphate), reduced form (NAD(P)H); flavin adenine dinucleotide, oxidized form (FAD); flavin adenine dinucleotide, reduced form ($FADH_2$); and oxygen (O_2) utilization.

44. The method of claim 36, wherein the metabolic pathway is monitored within the population of cells, said monitoring comprising measuring a physico-chemical parameter that is related to the glycolytic pathway, wherein said parameter comprises a stoichiometric or highly correlated relationship with glucose concentration.

45. The method of claim 36, wherein the population of cells comprises a predominantly oxidative metabolism or can be induced to comprise a metabolism predominantly based on oxidative phosphorylation.

46. The method of claim 45, wherein the metabolic pathway is monitored within the population of cells, said monitoring comprising measuring a metabolite or analyte that is generated as a result of the oxidative metabolic pathway, wherein said metabolite or analyte comprises a stoichiometric or highly correlated relationship with glucose concentration.

47. The method of claim 45, wherein the metabolic pathway is monitored within the population of cells, said monitoring comprising measuring a physico-chemical parameter that is generated as a result of the oxidative metabolic pathway and that comprises a stoichiometric or highly correlated relationship with glucose concentration.

48. A noninvasive method for monitoring *in vivo* blood glucose levels, the method comprising:

applying at least one small molecule metabolic reporter (SMMR) to at least one surface of skin for a predetermined period of time;

causing penetration of the one or more SMMR to a depth of about 10 μm, wherein said depth corresponds with the bottom of the dead stratum corneum layer, to about 175 μm, wherein said depth corresponds with the top of the dermal layer, into the epidermis;

contacting the one or more SMMR with one or more metabolites or analytes;

monitoring a change in the concentration of the one or more metabolites or analytes by detecting changes in the SMMR using an optical reader, and

correlating the change in the concentration of the one or more metabolites or analytes with *in vivo* blood glucose levels.

49. The method of claim 48, wherein the at least one small molecule metabolic reporter is selected from the group consisting of a fluorophore, a protein labeled fluorophore, a protein comprising a photooxidizable cofactor, a protein comprising another intercalated fluorophore, a mitochondrial vital stain or dye, and a dye exhibiting one or more of a redox potential, a membrane localizing dye, a dye comprising energy transfer properties, a pH indicating dye, a coumarin dye, a derivative of a coumarin dye, an anthraquinone dye; a cyanine dye, an azo dye; a xanthene dye; an arylmethine dye; a pyrene derivative dye and a ruthenium bipyridyl complex dye.

50. The method of claim 48, wherein the one or more specific metabolites are selected from the group consisting of glucose, lactate, H^+, Ca^{2+}, Mg^{2+}, Na^+, K^+, ATP, ADP, P_i, glycogen, pyruvate, NAD(P)+, NAD(P)H, FAD, $FADH_2$, and O_2.

51. The method of claim 49, wherein the protein labeled fluorophore is Glucose Oxidase-Labeled Fluorophore (GO-LF) and the metabolite is glucose.

52. The method of claim 49, wherein the protein comprising a photooxidizable cofactor is Glucose Oxidase (GOx) with a flavin adenine dinucleotide (FAD) in the triplet state (GOx-^{3}FAD*).

53. The method of claim 49, wherein the mitochondrial vital stain or dye is at least one polycyclic aromatic hydrocarbon dye selected from the group consisting of: Rhodamine 123, Di-4-ANEPPS; Di-8-ANEPPS, $DiBAC_4(3)$, RH421, Tetramethylrhodamine ethyl ester, perchlorate, Tetramethylrhodamine methyl ester, perchlorate, 2-(4-(dimethylamino)styryl)-*N*-ethylpyridinium iodide, 3,3'-Dihexyloxacarbocyanine, 5,5',6,6'-tetrachloro-1,1',3,3' -tetraethyl-benzimidazolylcarbocyanine chloride, 5,5',6,6'-tetrachloro-1,1',3,3' -tetraethyl-benzimidazolylcarbocyanine iodide, Nonylacridine Orange, Dihydrorhodamine 123 and Dihydrorhodamine 123, dihydrochloride salt; xanthene; 2',7'-bis-(2-carboxyethyl)-5-(and-6)-carboxyfluorescein; benzenedicarboxylic acid; 2(or 4)-[10-(dimethylamino)-3-oxo-3-H-benzo[c]xanthene-7-yl]; and iodine dissolved in potassium iodide.

54. The method of claim 49, where monitoring the change in the one or more metabolite or analyte concentrations comprises measuring at least one spectral emission at a wavelength above 450 nm.

55. A reagent strip for use in a glucose measuring instrument comprising:

a polymer strip; and

a known concentration of at least one small molecule metabolic reporter (SMMR),

wherein when a sample of a biological fluid containing an amount of glucose is interacted with the reagent strip, a change in fluorescence or absorption of the at least one SMMR occurs, wherein said change is measured by the glucose measuring instrument, thereby detecting the glucose concentration of the biological fluid.

56. The reagent strip of claim 55, wherein the at least one SMMR is selected from the group consisting of Glucose Oxidase-Labeled Fluorophore (GO-LF) and Glucose Oxidase (GOx) with a flavin adenine dinucleotide (FAD) in the triplet state (GOx-^{3}FAD*).

57. The reagent strip of claim 55, wherein the change in fluorescence or absorption is monitored using fluorescence or absorption spectroscopy.

58. A reagent strip for use in calibrating a glucose measuring instrument comprising:

a polymer strip;

a known concentration of at least one small molecule metabolic reporter (SMMR); and

at least one sample containing a known concentration of glucose,

wherein when the at least one sample is interacted with the reagent strip, a change in fluorescence or absorption of the at least one SMMR occurs, wherein said change is measured by the glucose measuring instrument and wherein the calculated glucose is compared to the known concentration, thereby calibrating the instrument.

59. The reagent strip of claim 58, wherein the at least one SMMR is selected from the group consisting of Glucose Oxidase-Labeled Fluorophore (GO-LF) and Glucose Oxidase (GOx) with a flavin adenine dinucleotide (FAD) in the triplet state (GOx-^{3}FAD*).

60. The reagent strip of claim 59, wherein the change in fluorescence or absorption is monitored using fluorescence or absorption spectroscopy.

61. A sensor system, the system comprising:

a device comprising a component that transmits radiation to a material or tissue, a component that detects radiation emitted from a material or tissue, and a component to display the detection results, wherein each component is operably linked;

an applicator that delivers the sensor composition of claim 1 to the material or tissue; and

an interface between the device and the material or tissue, wherein the interface measures a resulting excitation radiation emitted from the irradiated sensor composition.

62. The sensor system of claim 61, wherein said system comprises a device that emits radiation at one or more wavelengths chosen to specifically excite the sensor composition that is applied to the material or tissue, wherein the sensor composition comprises at least one small molecule metabolic reporter (SMMR), wherein the sensor composition is present at a depth from the surface of the skin of about 10 μm, wherein said depth corresponds with the bottom of the dead stratum corneum layer, to about 175 μm, wherein said depth corresponds with the top of the dermal layer, in the epidermis at an effective concentration for detection of one or more metabolites or analytes in a biological sample.

63. The sensor system of claim 62, wherein said system detects radiation at one or more wavelengths chosen to specifically identify remitted energy fluorescence scattered to the system from the sensor composition.

64. A method for determining *in vivo* blood glucose concentration, comprising the steps of:

performing an instrument response measurement on a calibration target and recording the response data;

applying at least one SMMR mixture to the skin in a first controlled area such that the SMMR resides in the epidermal layer of the skin;

applying a second SMMR mixture to the skin in a second controlled area;

perturbing the second area such that one or more extreme changes that the mixture may undergo are achieved;

performing a calibration measurement on the perturbed area and recording the calibration data;

performing a background measurement on an area of skin that has no SMMR and recording this background data;

illuminating the first area with light and performing a first measurement on the first area;

detecting at least one wavelength spectrum of light reflected back from the first area;

performing at least a second measurement on the first area at wavelengths suitable for each SMMR present;

calculating at least one parameter from the response data to normalize the background data, calibration data and measurement data for the response using a spectrometer;

calculating at least one parameter from the background data to correct the calibration data and measurement data for emission, absorption and scattering properties of the tissue; and

calculating at least one metabolite parameter from the calibration data to relate the measurement data to the blood glucose concentration;

thereby determining *in vivo* blood glucose concentration.

65. The method of claim 64, wherein the one or more extreme changes is a change in concentration of the metabolite or analyte between a zero or low measurable concentration and a saturation level or high measurable concentration.

66. A method of calculating a blood glucose concentration, said method comprising:

measuring at least one background response and at least one autofluorescence tissue response from a calibration target comprising an epidermal layer of skin;

providing a first SMMR mixture to a first skin location and causing portions of the first SMMR mixture to transfer into the epidermal layer of the skin;

providing a second SMMR mixture to a second skin location and causing and recording at least one extreme change in the mixture;

illuminating the first skin location with a radiative emission;

detecting at least one resulting wavelength spectrum reflected from the first skin location;

optionally repeating the illuminating and detecting steps using at least one irradiation and wavelength spectrum associated with each SMMR provided; and

detecting at least one physico-chemical parameter that is related to the glycolytic pathway, wherein said parameter comprises a stoichiometric or highly correlated relationship with glucose concentration;

thereby determining the blood glucose concentration.

67. The method of claim 66, wherein the SMMR mixture comprises a bloodless calibration procedure as outlined in one or more of equations 13, 16, 17, 18, 19, 20 or 21.

68. The method of claim 66, wherein the at least one extreme change is a change in the blood glucose concentration between a zero or low measurable concentration and a saturation level or high measurable concentration.

69. A method for determining the concentration of at least one metabolite or analyte in skin tissue, the method comprising:

administering to the skin tissue at least one small molecule metabolite reporter (SMMR) agent;

causing penetration of the at least one SMMR agent to a region of the skin at a depth between the dermis and the epidermis, wherein the depth from the surface of the skin is from

about 10 μm, wherein said depth corresponds with the bottom of the dead stratum corneum layer, to about 175 μm, wherein said depth corresponds with the top of the dermal layer;

irradiating the at least one SMMR agent in the skin tissue with a source of electromagnetic radiation;

measuring at least one fluorescence spectrum emitted from the at least one SMMR agent; and

analyzing the emitted fluorescence spectra;

wherein the analysis results in a determination of the concentration of the metabolite or analyte.

70. The method of claim 63, wherein the measuring of at least one fluorescence spectrum comprises a bloodless calibration procedure as outlined in one or more of equations 13, 16, 17, 18, 19, 20 and 21.

71. The method of claim 32, where monitoring the change in metabolite or analyte concentration comprises detecting at least one wavelength above 450 nm.